

REMARKS

1. Status of Claims

Claims 9, 13–30 and 32–33 are canceled.

Claims 1, 5–7, 10, 12 and 31 are currently amended.

New claims 34–50 are added.

Claims 1–8, 10–12, 31 and 34–50 are pending.

2. Claim Rejections Under 35 U.S.C. § 112, First Paragraph

A. **"Inhibition."** Claims 1–8, 10–12 and 31 are rejected in the Office Action of June 2, 2006 as lacking enablement in the specification for the full scope of the claims. The Office Action acknowledges that the claims are enabled for reducing proliferation of a cell expressing Janus tyrosine kinase 3 (Jak3) or suppressing an undesired function of a cell expressing Jak3 with a compound represented by the formula I, or a salt thereof. It is said, however, that the specification does not reasonably provide enablement for "inhibiting function and/or proliferation of a cell expressing Jak3. It is also said that enablement is lacking for suppressing an undesired function of a cell expressing Jak3 with a metabolite or a precursor.

In the interest of advancing prosecution, Applicants currently amend independent claims 1 and 31 to recite "suppressing," instead of "inhibiting," a function or an undesired function. In order to simplify the issues, claims 1 and 31 are also currently amended to delete "and/or proliferation of a cell," in favor of reintroducing the limitation "reducing proliferation of a cell" in new dependent claims 34 and 39, respectively.

Notwithstanding the amendments, Applicants do not agree with any suggestion that "inhibition of proliferation of a cell expressing Jak3" refers to only "the preventive measure or total inhibition."¹ As shown in Figs. 1A-B, and in the specification², various concentrations of the representative 649641P compound (also called NC1153) caused the percent (%) inhibition of T-cell proliferation to vary over the full range of 0–100% inhibition. One of ordinary skill in the art would have understood at the time the present application was filed that "inhibition of cell proliferation," as disclosed in the present specification, encompasses partial inhibition and total inhibition.

B. **"A Metabolite" or "a Precursor."** As to claim 10, it is said in the Office Action that the instant specification does not provide sufficient guidance in how to make/use "a metabolite" or "a

¹ Office Action dated June 2, 2006, Detailed Action, pg. 4, ll. 7–9 and 20; pg. 5, ll. 10 and 17.

² Specification paragraphs [0061]–[0062], for example.

precursor" of the compounds recited in claim 1. Applicants are currently amending claim 10 to omit reference to metabolite, derivative and precursor, without waiving the right to reintroduce those limitations later in a related or continuation application.

3. Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 6, 12 and 31 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. It is said that the term "substantially" (claim 6) is a relative term that lacks a standard for ascertaining the requisite degree and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Applicants believe that a person of ordinary skill in the art would understand the meaning of "substantially non-inhibitory." Nevertheless, in the interest of advancing prosecution by reducing the issues in controversy, Applicants currently amend claim 6 to omit "substantially," and to require instead that the compound is "non-inhibitory or is less inhibitory" of protein tyrosine kinase activity other than Jak3. This amendment is supported in the specification, at paragraph [0076], for example.

The terms "continuously" and "periodically" (claim 12) are also said in the Office Action to lack a standard for ascertaining the requisite degree and the skilled person would not be reasonably apprised of the scope of the invention. Applicants respectfully disagree, and submit that the ordinarily skilled person would have understood "continuously administering" to mean administration "marked by uninterrupted extension in space, time, or sequence: continuing without intermission or recurring regularly after minute interruptions".³ Applicants also submit that the ordinarily skilled person would have understood "periodic administration" to mean administration "occurring or recurring at regular intervals".⁴ Applicants are currently amending claim 12 to delete "periodically," and are introducing that limitation in new claim 35, in order to sever the issues of "periodic" and "continuous" administration, should any controversy remain with respect to either of those terms.

As to claim 31, the phrase "at least one compound of the formula..." is said to be inconsistent with the single compound recited. Claim 31 is currently amended to delete "at least one."

³ MedlinePlus® Merriam-Webster [online]. Retrieved from the Internet:<URL: <http://www2.merriam-webster.com/cgi-bin/mwmednlm?book=Medical&va=continuous>. Printed September 18, 2006 (copy attached).

⁴ MedlinePlus® Merriam-Webster [online]. Retrieved from the Internet:<URL: <http://www2.merriam-webster.com/cgi-bin/mwmednlm?book=Medical&va=periodic>. Printed September 18, 2006 (copy attached).

4. Claim Rejections Under 35 U.S.C. § 102(b) - *Dimmock*.

Claims 1–6, 9 and 31 are rejected under 35 U.S.C. § 102(b) as being anticipated by *Dimmock et al.* (Pharmazie, 1995, 50(1), 668–71) (hereinafter, *Dimmock*). It is said in the Office Action that *Dimmock* teaches a compound according to Applicants' claim 1 as a cytotoxic agent tested against murine P388 D1 lymphocytic leukemia cells. The Office takes the position that each characteristic or property recited in Applicants' claims 1–6, 8 and 31 must be inherent to *Dimmock* since the administration of the same compound in overlapping dosage amounts to a lymphoid cell would inherently provide the claimed utility.

Applicants are currently amending claims 1 and 31 to require a step of selectively targeting Jak3 activity in the cell for inhibition and to require that the outcome of the method is the suppression of a Jak3-dependent function of the cell. The amendments are supported in the Specification at paragraph [00108], for example. As discussed above, claims 1 and 31 have been amended for the purpose of simplifying and separating issues, and no longer recite "and/or proliferation of said cell is inhibited." Applicants respectfully submit that the method of each of claims 1–6, 8 and 31 constitutes a new use of any Mannich base that may have been previously employed by *Dimmock*.

All Limitations not Taught by *Dimmock*. An "anticipating" reference must describe all of the elements and limitations of the claim in a single reference, and enable one of skill in the field of the invention to make and use the claimed invention (*Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, 246 F.3d 1368, 1378-79 (Fed. Cir. 2001)). With respect to claims 1 and 31, at least the step of selectively inhibiting Jak3 activity and the outcome of the method ("whereby a Jak3-dependent function of said cell is suppressed") are not found in *Dimmock*.

Limitations Not Inherent in *Dimmock*.

In order to show inherency, the Examiner must "provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic *necessarily flows* from the teachings of the applied prior art." *MPEP* § 2112 (2005) (citing *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990)) (Emphasis added). It is not sufficient for the Examiner merely to show that "a result or characteristic *may occur or be present* in the prior art." *MPEP* § 2112 (citing *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993)) (Emphasis added). Claims 1 and 31 each provide a way to target and selectively inhibit Jak3 activity in any Jak3-expressing cell, whereas *Dimmock* is directed to killing leukemia cells by sequential administration of certain Mannich bases to achieve greater toxicity to malignant cells than normal

cells.⁵ There is no reasonable basis for assuming, and the Office has not shown such a basis, that the murine P388D1 leukemia cells would have necessarily and unavoidably expressed Jak3 under the testing conditions employed by *Dimmock*. One of ordinary skill in the art, given the *Dimmock* disclosure, would not have been placed in possession of the claimed method of claims 1–6, 8 and 31. The idea of selectively inhibiting Jak3-dependent activity in a cell was not even contemplated in *Dimmock*, much less any teaching of using such selective inhibition to suppress an undesired Jak3-dependent cell function. This is true even if the cell were of lymphoid or myeloid origin (claim 4). There is no teaching in *Dimmock* of manipulating the signal 3 pathway in a cell (claim 5). *Dimmock* does not teach inhibiting Jak3 activity in a cell to a greater extent than it inhibits other protein tyrosine kinases (*e.g.*, Jak2) (claim 6). To the contrary, *Dimmock* teaches a different use of certain Mannich bases which involves "sequential cytotoxicity," the sequential administration of various Mannich bases as a way of causing greater toxicity to malignant cells than to normal tissue. The Office Action acknowledges that "...*Dimmock* is silent about the activity of said compound in 'inhibiting function and/or proliferation of a cell expressing Janus tyrosine kinase 3'." There is no teaching in *Dimmock* regarding any Jak3 expression in P388D1 mouse leukemia cells.

The Supreme Court long ago established in *Tilghman v. Proctor*, 102 U.S. 707–735 (1880) that it would be "absurd" to hold that a patent is anticipated because those skilled in the art later recognize that the discovery was "accidentally and unwittingly produced whilst the operators were in pursuit of other and different results, without exciting attention and without its even being known what was done or how it had been done." *See also Eibel Process Co. v. Minn & Ont. Paper Co.*, 261 U.S. 45, 66 (1923) ("[A]ccidental results, not intended and not appreciated, do not constitute anticipation."). With respect to the instant matter, despite any inherent properties of any of the Mannich bases of *Dimmock*, the method described by *Dimmock* would not have placed the skilled person in possession of a way to selectively interfere with the signal 3 pathway in cells that are expressing Jak3, or of a method to selectively inhibit the Jak3 enzyme.

In *Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc.*, the CAFC affirmed that new uses of known processes may be patentable. *See* 35 U.S.C. § 101 (1994) ("Whoever invents or discovers any new and useful process, art or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material."). In *Bristol-Myers*, the claimed process was not directed to a new use; it was found to be the same use, and it consisted of the same steps as described

⁵ *Dimmock*, pg. 668, second column, first paragraph.

by the anticipating reference. The court stated that "[n]ewly discovered results of known processes directed to the same purpose are not patentable because such results are inherent." [emphasis added]. In contrast to the circumstances in the *Bristol-Meyers* case, the instant claims 1–6, 8 and 31 are directed to a different purpose than that of *Dimmock*.

Because all of the limitations of each of claims 1–6, 9 and 31 are not found, expressly or inherently, in *Dimmock*, withdrawal of this rejection is respectfully requested.

5. Claim Rejections Under 35 U.S.C. § 102(b) - *Chimie et Atomistique*.

Claims 1, 4, 5, 6, 7, 8 and 10–11 are rejected under 35 U.S.C. § 102(b) as being anticipated by *Chimie et Atomistique* (FR 1466205 or CA712187) (hereinafter, *Chimie*). *Chimie* describes certain 12-carbon ring based compounds that are said to be useful as choleretic agents (bile stimulating agents). It is said in the Office Action that the characteristics or properties recited in Applicants' claims 1, 4, 5, 6, 7, 8 and 10–11 must be inherent in *Chimie* since the administration of the same compound in overlapping dosage amount to a rat would inherently provide the claimed utility.

Applicants respectfully traverse this rejection for at least the reason that, despite any similarity of any compound disclosed therein to any compound recited in Applicants' claim 1, 4–8, 10, or 11, the use disclosed by *Chimie* is markedly different than that of Applicants' claimed method. *Chimie* is directed to certain chemical agents for eliciting a prolonged choleretic effect in rat, with low toxicity. With respect to Applicants' independent claims 1 and 10, at least the step of selectively inhibiting Jak3 activity and the outcome of the method ("whereby a Jak3-dependent function of said cell is suppressed") are not found in *Chimie*. Any inherent properties or characteristics of the *Chimie* compounds would merely be accidentally and unwittingly produced while the operators were in pursuit of other and different results, without exciting attention and without its even being known what was done or how it had been done. The Office Action acknowledges that "...*Chimie* is silent about the activity of said compound in 'inhibiting function and/or proliferation of a cell expressing Janus tyrosine kinase 3'." For reasons similar to those set forth above with regard to the rejection of claim 1 over *Dimmock*, Applicants respectfully submit that all of the limitations of each of claims 1, 4–8, 10, or 11 are not found, expressly or inherently, in *Chimie*, and withdrawal of this rejection is respectfully requested.

6. Claim Rejections Under 35 U.S.C. § 103(a) - *Chimie et Atomistique*.

Claim 12 is rejected under 35 U.S.C. § 103(a) as being obvious in view of *Chimie et Atomistique* (FR 1466205 or CA712187) (*Chimie*). While acknowledging that *Chemie* differs from the claimed method in the continuously or periodically administering of the compound, the Office Action takes the position that the skilled person would have readily optimized effective concurrent administration regimes as determined by good medical practice and the clinical condition of the individual patient. It is said that determination of the appropriate administration regimens for treatment is routinely made by those of ordinary skill in the art and is within the ability of tasks routinely performed by them without undue experimentation, absent evidence to the contrary.

Applicants respectfully traverse the rejection of claim 12 for at least the reason that, even if the skilled person would be able to develop a suitable continuous or periodic administration regime for an individual patient, this does not make up for the failure of *Chemie* to teach the method of claim 10, from which claim 12 depends. The teaching of *Chemie* would merely lead the skilled person to devise a suitable continuous or periodic scheme for administering the compounds (choleretic agents) disclosed therein to a subject for the purpose of stimulating the production of bile by the liver.

Additional Claim Amendments

New dependent claims 34 and 39 have been added to recite, as a further limitation of claim 1 and 31, respectively, "wherein suppressing at least one Jak3-dependent function of said cell reduces proliferation of said cell." These claims distinguish over the cited references for at least the same reason as claims 1 and 31.

New claim 35, which depends from claim 10, is added to recite the limitation "periodically," which was deleted from claim 12 in order to sever the issues of "periodic" and "continuous" administration, should any controversy remain with respect to either of those terms.

New claim 36 is supported in the specification at paragraph [0102], for example, and is included to better ensure coverage of specific embodiments to which Applicants are entitled.

New claim 37 depends from claim 11 and requires that blocking cell division in a plurality of T-cells provides T-cell mediated immunosuppression. This claim is supported in the Specification at paragraphs [0024]-[0025], for example.

New claim 38 depends from claim 10 and requires that suppression of the undesired Jak3-dependent cell function comprises interfering with the signal 3 pathway in the cell. Support for this claim is found in original claim 5 and at paragraph [0025], for example, in the Specification.

Application No.: 10/731,769
Response to Office Action dated June 2, 2006

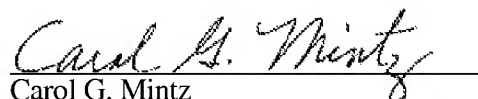
New claims 40-50 depend from claim 1 and each recites subgroups of the formula (I) compounds. These claims are submitted to simplify and separate any remaining or potential issues regarding particular formula (I) compounds.

No new matter is introduced by way of these amendments, and the new claims are properly included with the elected claims of Group (I)(a).

Conclusion

Reconsideration of this application and withdrawal of the rejections and objections are requested in light of the foregoing amendments and remarks. Applicants request allowance of all pending claims. This is believed to be a full and complete response to the Office Action dated June 2, 2006. If any issue in the Office Action has been overlooked or is deemed to be incompletely addressed, Applicants respectfully request the opportunity to supplement this response. It is believed that no extensions of time or fees are required, beyond those that may otherwise be provided for in documents accompanying this paper. In the event that any additional extension of time is necessary to allow consideration of this paper, such extension is hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required (including fees for net addition of claims) are hereby authorized to be charged to Deposit Account Number 03-2769 of Conley Rose, P.C., Houston, Texas.

Respectfully submitted,



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Attachments: MedlinePlus® Medical Dictionary (2 pages).

Medical Dictionary

4 entries found for **continuous**. Select an entry and then click 'Go'.

continuous

continuous phase
continuous positive airway pressure
dispersion medium

Main Entry: **con·tin·u·ous**
Pronunciation: ken-'tin-yə-wəs

Function: *adjective*

: marked by uninterrupted extension in space, time, or sequence :
continuing without intermission or recurring regularly after minute
interruptions <continuous vitamin injections>

- **con·tin·u·ous·ly** *adverb*

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Pronunciation Key

\ ə \ as a in abut	\ ɡ \ as g in go	\ r \ as r in red
\ ˈə ɪə \ as u in abut	\ h \ as h in hat	\ s \ as s in less>
\ ɪ \ as e in kitten	\ ɪ \ as i in hit	\ sh \ as sh in shy
\ ər \ as ur/er in further	\ ɪ \ as i in ice	\ t \ as t in tie
\ a \ as a in ash	\ j \ as j in job	\ th \ as th in thin
\ ă \ as a in ace	\ k \ as k in kin	\ ʰ \ as th in the
\ ă \ as o in mop	\ ʃ \ as ch in ich dien	\ ū \ as oo in loot
\ aʊ \ as ou in out	\ ɪ \ as i in lily	\ ū \ as oo in foot
\ b \ as in baby	\ m \ as m in murmur	\ v \ as v in vivid
\ ch \ as ch in chin	\ n \ as n in own	\ w \ as w in away
\ d \ as d in did	\ ŋ \ as ng in sing	\ y \ as y in yet
\ e \ as e in bet	\ ɔ \ as o in go	\ yū \ as you in youth
\ ˈē ɪē \ as ea in easy	\ ɔ \ as aw in law	\ yū \ as u in curable
\ ē \ as y in easy	\ ɔɪ \ as oy in boy	\ z \ as z in zone
\ f \ as f in fifty	\ p \ as p in pepper	\ zh \ as si in vision

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Medical Dictionary

8 entries found for **periodic**. Select an entry and then click 'Go'.

periodic	Go
moon blindness	
periodic acid	
periodic acid-Schiff	
periodic breathing	
periodic law	

Main Entry: **pe-ri-od-ic**

Pronunciation: **pīr-ē-'ād-ik**

Function: *adjective*

: occurring or recurring at regular intervals <*periodic* epidemics>

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Pronunciation Key

\ ə \ as a in abut	\ g \ as g in go	\ r \ as r in red
\ 'ə \ as u in abut	\ h \ as h in hat	\ s \ as s in less>
\ ə \ as e in kitten	\ i \ as i in hit	\ sh \ as sh in shy
\ ər \ as ur/er in further	\ ī \ as i in ice	\ t \ as t in tie
\ a \ as a in ash	\ j \ as j in job	\ th \ as th in thin
\ ā \ as a in ace	\ k \ as k in kin	\ th \ as th in the
\ ä \ as o in mop	\ k̄ \ as ch in ich dien	\ ū \ as oo in loot
\ aũ \ as ou in out	\ l \ as l in lily	\ ũ \ as oo in foot
\ b \ as b in baby	\ m \ as m in murmur	\ v \ as v in vivid
\ ch \ as ch in chin	\ n \ as n in own	\ w \ as w in away
\ d \ as d in did	\ ŋ \ as ng in sing	\ y \ as y in yet
\ e \ as e in bet	\ ō \ as o in go	\ yū \ as you in youth
\ 'ē \ as ea in easy	\ ȯ \ as aw in law	\ yũ \ as u in curable
\ ē \ as y in easy	\ ȱ \ as oy in boy	\ z \ as z in zone
\ f \ as f in rify	\ p \ as p in pepper	\ zh \ as si in vision

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